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☐ 1: Eur J Biochem 2000 Oct;267(20):6140-50

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## Cloning, expression and chromosomal localization of a novel human dipeptidyl peptidase (DPP) IV homolog, DPP8.

Abbott CA, Yu DM, Woollatt E, Sutherland GR, McCaughan GW, Gorrell MD.

A. W. Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Centenary Institute of Cancer Medicine and Cell Biology and The University of Sydney, NSW, Australia. c.abbott@centenary.usyd.edu.au

Dipeptidyl peptidase (DPP) IV has roles in T-cell costimulation, chemokine biology, type-II diabetes and tumor biology. Fibroblast activation protein (FAP) has been implicated in tumor growth and cirrhosis. Here we describe DPP8, a novel human postproline dipeptidyl aminopeptidase that is homologous to DPPIV and FAP. Northern-blot hybridization showed that the tissue expression of DPP8 mRNA is ubiquitous, similar to that of DPPIV. The DPP8 gene was localized to chromosome 15q22, distinct from a closely related gene at 19p13.3 which we named DPP9. The full-length DPP8 cDNA codes for an 882-amino-acid protein that has about 27% identity and 51% similarity to DPPIV and FAP, but no transmembrane domain and no N-linked or O-linked glycosylation. Western blots and confocal microscopy of transfected COS-7 cells showed DPP8 to be a 100-kDa monomeric protein expressed in the cytoplasm. Purified recombinant DPP8 hydrolyzed the DPPIV substrates Ala-Pro, Arg-Pro and Gly-Pro. Thus recombinant DPP8 shares a postproline dipeptidyl aminopeptidase activity with DPPIV and FAP. DPP8 enzyme activity had a neutral pH optimum consistent with it being nonlysosomal. The similarities between DPP8 and DPPIV in tissue expression pattern and substrates suggests a potential role for DPP8 in T-cell activation and immune function.

### MeSH Terms:

- Amino Acid Sequence
- Antigens, CD26/genetics\*
- Antigens, CD26/chemistry
- Cell Line
- Chromosome Mapping

- Chromosomes, Human, Pair 15\*
- Chromosomes, Human, Pair 19
- Cloning, Molecular
- Growth Substances/chemistry
- Human
- Lymphocytes/enzymology
- Molecular Sequence Data
- Monocytes/enzymology
- Recombinant Proteins/chemistry
- Recombinant Proteins/biosynthesis
- Sequence Alignment
- Sequence Homology, Amino Acid
- Serine Endopeptidases/chemistry
- Support, Non-U.S. Gov't

## Substances:

- Serine Endopeptidases
- Antigens, CD26
- fibroblast-activating factor
- Recombinant Proteins
- Growth Substances

## Secondary source id:

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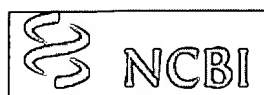
PMID: 11012666 [PubMed - indexed for MEDLINE]

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☐ 1: AF221634. Homo sapiens dipe...[gi:11095187]

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 and Gorrell,M.D.  
 TITLE Cloning, expression and chromosomal localization of a novel human  
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 JOURNAL Eur. J. Biochem. 267 (20), 6140-6150 (2000)  
 MEDLINE 20467194  
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 AUTHORS Abbott,C.A., Yu,D., McCaughan,G.W. and Gorrell,M.D.  
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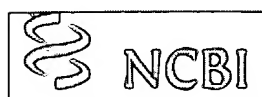
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☐ 1: AF221635. Homo sapiens dipe...[gi:11095189]

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 TITLE Cloning, expression and chromosomal localization of a novel human dipeptidyl peptidase (DPP) IV homolog, DPP8  
 JOURNAL Eur. J. Biochem. 267 (20), 6140-6150 (2000)  
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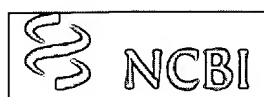
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☐ 1: AF221636. Homo sapiens dipe...[gi:11095191]

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 TITLE Cloning, expression and chromosomal localization of a novel human dipeptidyl peptidase (DPP) IV homolog, DPP8  
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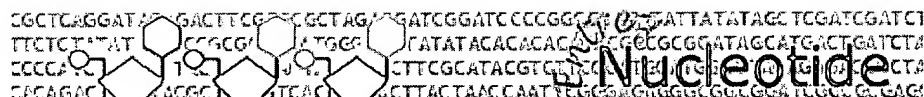
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781 tccacactgt gtgtcccttt acaagctatc aagtcctgaa gatgacccaa cttgcaaaac
841 aaaggaatth tggggccacca ttttgattc agcaggctct cttcctgact atactcctcc
901 agaaatthtc tcttttgaaa gtactactgg atttacattg tatgggatgc tctacaagcc
961 tcatgatcta cagcctggaa agaaatatcc tactgtgctg ttcatatatg gtggctcctca
1021 ggttgctatt gctggggccc cagtcactct gtggatcttc tatgatacag gatacacgga
1081 acgttatatg ggtcacctcg accagaatga acagggtctat tacttaggat ctgtggccat
1141 gcaagcagaa aagttccctt ctgaaccaa tctgttactg ctcttacatg gtttcctgga
1201 tgagaatgtc cttttgcac ataccagtat attactgagt tttttagtga gggctggaaa
1261 gccatatgat ttacagatct atcctcagga gagacacagc ataagagttc ctgaatcggg
1321 agaacattat gaactgcac ttttgacta ctttcaagaa aaccttggat cacgtattgc
1381 tgctctaaaa gtgatataat tttgacctgt gtagaactct ctggtataca ctggctatth
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1501 tgccatgtaa catctactcc tgaaaataaa tgtgggtgcca tgcaggggtc tacggtttgt
1561 ggtagtaatc taatacctta accccacatg ctcaaaatca aatgatacat attcctgaga
1621 gaccagcaa taccataaga attactaaaa aaaaaaaaaa aaaaaaaaaa
```

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Boo

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## Details

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LOCUS       AF221637                1083 bp      mRNA      linear      PRI 05-NOV-2000
DEFINITION  Homo sapiens dipeptidyl peptidase 8 (DPP8) mRNA, partial cds,
alternatively spliced.
ACCESSION   AF221637
VERSION     AF221637.1   GI:11095193
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1 (bases 1 to 1083)
AUTHORS     Abbott,C.A., Yu,D.M., Woollatt,E., Sutherland,G.R., McCaughan,G.W.
            and Gorrell,M.D.
TITLE       Cloning, expression and chromosomal localization of a novel human
            dipeptidyl peptidase (DPP) IV homolog, DPP8
JOURNAL      Eur. J. Biochem. 267 (20), 6140-6150 (2000)
MEDLINE      20467194
PUBMED       11012666
REFERENCE   2 (bases 1 to 1083)
AUTHORS     Abbott,C.A., Yu,D., McCaughan,G.W. and Gorrell,M.D.
TITLE       Direct Submission
JOURNAL      Submitted (06-JAN-2000) A.W. Morrow Gastroenterology and Liver
            Centre, Centenary Institute of Cell Biology and Cancer Medicine,
            Locked Bag No.6, Newtown, Sydney, NSW 2042, Australia
FEATURES             Location/Qualifiers
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                        /db_xref="taxon:9606"
                        /chromosome="15"
                        /map="15q22"
                        /clone="stPBMCd3-3-1"
                        /cell_type="PHA stimulated PBMC"
     gene            1..1083
                        /gene="DPP8"
     CDS            1..1083
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                        /note="serine protease; member of prolyl oligopeptidase S9b
                        family belonging to enzyme clan SC; additional splice
                        variants of this mRNA are found in GenBank Accession
                        Numbers AF221634, AF221635 and AF221636"
                        /codon_start=2
                        /product="dipeptidyl peptidase 8"
                        /protein_id="AAG29769.1"
                        /db_xref="GI:11095194"
                        /translation="EEDARSAGVATFVLQEEFDRLSYGWWCPKAETTPSGGKILRLIY
                        EENDESEVEIIHVTSPMLETRRADSFYPKTGTTANPKVTFKMSEIMIDAEGRIIVDEV
                        RRLVYFEGTKDSPLEHHLYVVSYPNPGEVTRLTDRGYSHSCCISOHCDFDFISKYSNOQ

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NPHCVSLYKLSSPEDDPTCKTKEFWATILDSAGPLPDYTPPEIFSFESTTGFTLYGML  
YKPHDLQPGKKYPTVLFYGGPQVQLVNNRFGVKYFRLNTLASLGYVVVVIDNRGSC  
HRGLKFEGAFKYKMGQIEIDDQVEGLQYLASRYDFIDLDRVGIHGWSYGGYLSLMALM  
QRSDIFRVAIAGAPVTLWIFYDTGYT"

BASE COUNT        312 a        213 c        247 g        311 t  
ORIGIN

```
1 ggaagaagat gccagatcag ctggagtcgc tacctttggt ctccaagaag aatttgatag
61 atattctggc tattggtggt gtccaaaagc tgaacaact cccagtgggt gtaaaattct
121 tagaattcta tatgaagaaa atgatgaatc tgaggtggaa attattcatg ttacatcccc
181 tatgttggaa acaaggaggg cagattcatt ccgttatcct aaaacaggta cagcaaattc
241 taaagtcact ttaagatgt cagaaataat gattgatgct gaaggaagga tcatagttga
301 tgaagtcaga aggctggtat attttgaagg caccaaagac tcccctttag agcatcacct
361 gtacgtagtc agttacgtaa atcctggaga ggtgacaagg ctgactgacc gtggctactc
421 acattcttgc tgcatcagtc agcactgtga cttctttata agtaagtata gtaaccagaa
481 gaatccacac tgtgtgtccc tttacaagct atcaagtcct gaagatgacc caacttgcaa
541 aacaaaggaa ttttgggcca ccattttgga ttcagcaggt cctcttcctg actatactcc
601 tccagaaatt ttctcttttg aaagtactac tggatttaca ttgtatggga tgctctacaa
661 gcctcatgat ctacagcctg gaaagaaata tcctactgtg ctgttcatat atggtggtcc
721 tcaggtgcag ttggtgaata atcggtttaa aggagtcaag tatttcgct tgaataccct
781 agcctctcta gggtatgtgg ttgtagtgat agacaacagg ggatcctgtc accgagggct
841 taaatttgaa ggcgccttta aatataaaat ggggtcaaata gaaattgacg atcaggtgga
901 aggactccaa tatctagctt ctcgatatga tttcattgac ttagatcgtg tgggcatcca
961 cggctggtcc tatggaggat acctctccct gatggcatta atgcagaggt cagatatctt
1021 cagggttgct attgctgggg cccagtcac tctgtggatc ttctatgata caggatacac
1081 gga
```

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[3.4.14.3 Transferred entry: now EC 3.4.19.1 - Acylaminoacyl-peptidase]

3.4.14.4      Dipeptidyl-peptidase III  
REACTION:      Release of an N-terminal dipeptide from a peptide of four or more residues, with broad specificity  
OTHER NAME(S):      Dipeptidyl aminopeptidase III; Dipeptidyl arylamidase III; Red cell angiotensinase; Enkephalinase B  
COMMENTS:      A cytosolic serine-type peptidase active at neutral pH. Highly selective for Arg-Arg-2-naphthylamide at pH 9.2. Inactive on (Glu)<sub>4</sub>, (Gly)<sub>4</sub>, and tripeptides, as well as bonds involving proline  
REFERENCES:      1237, 3197, 4862

3.4.14.5      Dipeptidyl-peptidase IV  
REACTION:      Release of an N-terminal dipeptide, Xaa-Xbb-Xcc, from a polypeptide, preferentially when Xbb is Pro, provided Xcc is neither Pro nor hydroxyproline  
OTHER NAME(S):      Dipeptidyl aminopeptidase IV; Xaa-Pro-dipeptidyl-aminopeptidase; Gly-Pro naphthylamidase; Postproline dipeptidyl aminopeptidase IV  
COMMENTS:      A membrane-bound serine-type peptidase in mammals and flavobacteria  
REFERENCES:      2478, 3192, 5345

3.4.14.6      Dipeptidyl-dipeptidase  
REACTION:      Preferential release of dipeptides from a tetrapeptide, e.g. Ala-Gly-Ala-Gly. Acts more slowly on Ala-Ala-Ala-Ala and Gly-Gly-Gly-Gly  
OTHER NAME(S):      Dipeptidyl tetrapeptide hydrolase; Dipeptidyl ligase; Tetrapeptide dipeptidase  
COMMENTS:      A thiol-activated peptidase from cabbage (*Brassica oleracea*). Tetrapeptides are formed from Ala-Ala, Gly-Gly, Ala-Gly and Gly-Ala  
REFERENCES:      1253

[3.4.14.7 Deleted entry: Tetralysine endopeptidase]

[3.4.14.8 Transferred entry: now EC 3.4.14.9 - Tripeptidyl-peptidase I and EC 3.4.14.10 - Tripeptidyl-peptidase II]

3.4.14.9      Tripeptidyl-peptidase I  
REACTION:      Release of an N-terminal tripeptide from a polypeptide  
OTHER NAME(S):      Tripeptidyl aminopeptidase; Tripeptidyl peptidase  
COMMENTS:      A lysosomal enzyme active at acidic pH. Inhibited by diisopropyl fluorophosphate. Formerly included in EC 3.4.14.8  
REFERENCES:      1111, 3194

3.4.14.10      Tripeptidyl-peptidase II  
REACTION:      Release of an N-terminal tripeptide from a polypeptide  
OTHER NAME(S):      Tripeptidyl aminopeptidase; Tripeptidyl peptidase  
COMMENTS:      A cytosolic enzyme active at neutral pH. Inhibited by diisopropyl fluorophosphate. Formerly included in EC 3.4.14.8  
REFERENCES:      275-6, 5066

Title: NOVEL SERINE PROTEASE GENES RELATED TO DPPIV

Inventors: Steve Qi et al.  
Attorney Docket No. 70669

DPP4 379 E.....CYRHICYFQIDKK....DCTFITKGTWEVIG....IEALTSDYLYYISNEYK  
DPRP1 473 SKYKRSSEGLEAPSDFKCPIK....EEIATITSGEWEVLGRHGSNIQVDEVRLVYFEGTK  
DPRP2 464 QGYDWSEPFSPGEDEFKCPK....EEIATITSGEWEVLGRHGSNIQVDEVRLVYFEGTK  
DPRP3 394 GR.....GEHHIAMLIQSKSEQITVRHITSGNWEVTK....IYAYDETTOKIYELSTE

DPP4 424 GMPGGRNLYKIQLSDYTKVTCISCELNPERCOYYSVSFSKEAKYIOLRCSGEGIPITYLH  
DPRP1 529 DSPLEHHLYVVSIVNPGEVTRLIDRCYSHSCCISCHCDFEITSKYSNOKNP.HCVSLYKLS  
DPRP2 520 DSPLEHHLYVVSIVNPGEVTRLIDRCYSHSCCISCHCDFEITSKYSNOKNP.HCVSLYKLS  
DPRP3 445 SSPRGRQLYSASTEGLLNRQCTISCNFMKEOCTYFDASFSPMNOHFLLECEGPRVPMVSLH

DPP4 484 SSVNDKGLRVLEDNSALDKMLQN..VOMPSKKLDFEILNETKFNOMILPHFDKSKKYP  
DPRP1 588 SPEDDPTCKTKEFWATILDSAGPLPDYTPPEIFSFESTTGETLYGMLYKPHDLQPGKKYP  
DPRP2 579 GPDDPLHNQPRFWASMMEAASCPDYMPPEIFHHTRSQVRLYGMITYKPHALQPGKKHP  
DPRP3 505 STDNPAKYFTLESNSMLKEAILKKKIGKE..EIKILHIDDYELPLQLSLPKDFMDRNOYA

DPP4 542 LHLDVYAGPCSOKADTVFR..LNWATYLASTENITVASFDGRGSGYQGDKIMHAINRRIG  
DPRP1 648 TMLFETGGPOVOLVNNRFKGMKYERLNTLASLGYMVVVIDNRGSGHRGLNFEAGAKYKMG  
DPRP2 639 TMLFVYGGPOVOLVNNRFKGMKYERLNTLASLGYMVVVIDNRGSGHRGLNFEAGAKYKMG  
DPRP3 563 LHLIMDEEPGGOLVTDKEH..IDWDSVLTMDNVIVAREFDGRGSGEGLKILQETERRIG

DPP4 600 TFEEDOMEFAARQFS..KMGFMDNKRITAIHGWSYGGYVTEMVLGSGSGVERKCGIAPVVR  
DPRP1 708 QTEEDOMEGLQYLASRYDFIDLDVGIHGWSYGGYLSLMALMORSDFEIVATAGAPVTL  
DPRP2 699 QVEEDOMEGLQYFAEKYGFIDISRVAIHGWSYGGYLSLMGLLHKPOVFNVAIAGAPVTV  
DPRP3 621 SVEKDDITAVKELL..KLPYIDSKRSLINCKGYGGYLSMILKSDEKIFKCGSVVAPTID

DPP4 659 WEYYDSVYTERYMGLPTPEDNLHYNSTVMSRAENFKOVEYLLIHGTADDNVHFQOQSAQ  
DPRP1 768 WLENDIGYTERYMGHDPDNEGGYLLGSSVAMQAEKFPSEPNRLLLIHGFLDENVHFAHTSI  
DPRP2 759 WMAVDIGYTERYMDVPENNOHGYEAGSVALHVEKLPNEPNRLLLIHGFLDENVHFEHINF  
DPRP3 680 LKLYASAFSERYTGMPSKEES..TYOASVILHNVHGLKEENTLIHGTADTKVHFQHSAE

DPP4 719 ISKALVDVGVDQAMWYTDDEHGLASSTAHQHIYTHMSHFTKOCFSLP.....  
DPRP1 828 LLSFLMRACKPYDLQIYPOERHSIRVPESGEHYELHLLHQLQENLGSRIAALKVI.....  
DPRP2 819 LNSQLMRACKPYDLQIYPOERHSIRVPESGEHYEVTLLHFLOEYL.....  
DPRP3 738 LKHLKLRACVNTMCMYPDGHNVSEK.SKYHLYSTILKFSDCLEETSVLPQEPEEDE

FIG. 1B

FOOTNOTES 429660